Research Topics

Our research is centered on acetylcholine functioning; with a focus on molecular biology and genomic applications to the study of cholinergic signaling, and especially on its microRNA regulation. Our work spans both basic and biomedical studies on cholinergic signaling in health and disease, particularly on anxiety-related topics.

MicroRNAs (miRNAs) rapidly emerge as global regulators of gene expression, yet the full scope of their roles in brain functioning is largely unknown. We combine advanced sequencing technologies with computational and transgenic engineering tools to investigate miRNA functions in the healthy and diseased brain, in particular acetylcholine-related processes. Our studies discovered cholinergic brain-to-body regulation of anxiety and inflammation and found "CholinomiRs", miRNA controllers of multiple cholinergic genes, several of them cloned and characterized in-house, that compete with each other on suppressing their targets. We test CholinomiR-based interventions with a focus on diseases involving impaired ACh signaling, anxiety, inflammation and neurodegeneration. In human volunteers, we find cholinergic-associated pulse increases under fear of terror; and elevated trait anxiety, blood pressure and inflammation under inherited interference with acetylcholinesterase (AChE)-targeting CholinomiRs. In stressed mice and engineered mice, we study cholinergic changes associated with CholinomiR increases under stress, inflammation and neurodegeneration, whereas in Alzheimer?s brains we see massive CholinomiRs decline, accompanying modifications in alternative splicing and transcript processing that differs from that of Parkinson?s disease and which may be reversed by antisense oligonucleotide treatment.

The Cholinergic System: From genes to neurotransmission

Acetylcholine (ACh) is the very first neurotransmitter to be discovered. It links the brain with body functions by performing what we define as Cholinergic Signalling.

Cholinergic stress responses

Relating cholinergic mechanisms to our stress-ful daily life: Notably, the impact of fear on our daily life in 2016 Israel increases the risk of disease; in a recent high-impact study with clinical experts, we combined machine learning with big data patient serum tests to explore this phenomenon.

Global Coevolution of Human MicroRNAs and Their Target Genes

MicroRNAs (miRNAs) have presumably contributed to the emergence of the novel expression patterns,
higher brain functions, and skills underlying human evolution. 

Read More [3]

Mouse models of cholinergic malfunctioning [4]
We have used transgenic mouse models with overexpressed cholinesterase variants as well as PD and AD models to study the involvement of cholinergic signaling in disease pathology and to define brain-to-body links that distinguish protective from damaging effects in specific pathogenic states.

Read More [4]

Pre-mRNA and post-transcriptional processing [5]
Pre-mRNA processing (and especially alternative splicing) is extensively used to achieve high molecular complexity, which sustains normal cognitive and behavioral functions and facilitates responses to altered internal and environmental conditions.

Read More [5]

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